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Patent
Attorney's Docket No. 020600-285

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Patent Application of)

SCHMIDT et al)

Application No.: 09/462,635)

Filed: April 10, 2000)

For: CATEGORISING NUCLEIC ACID)

Group Art Unit: 1655

Examiner: J. A. Goldberg

Confirmation No. 5341

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AMENDMENT AND REPLY PURSUANT TO 37 C.F.R. § 1.116

Assistant Commissioner for Patents
Washington, D.C. 20231

Sir:

In complete response to the Final Official Action mailed on December 21, 2001, in connection with the above-identified application, applicants provide the following amendments and remarks.

In The Claims:

Please replace claim 14 as follows:

14. (Twice Amended) A method for categorizing nucleic acid, wherein said method comprises:

(i) digesting double-stranded nucleic acid with an endonuclease to produce a nucleic acid population, wherein said endonuclease is selected such that each nucleic acid in the resulting nucleic acid population has a sticky end of a known base sequence and of a

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contd known common length extending from a terminal of its double-stranded portion, and wherein each nucleic acid in the nucleic acid population has a double-stranded portion; (ii) contacting the nucleic acid population with an adaptor to ligate the adaptor to a terminal of each nucleic acid in the nucleic acid population, wherein said adaptor comprises a double-stranded primer portion having a known base sequence, and a single-stranded portion complementary to the known sticky end of the nucleic acids in the nucleic acid population;

(iii) categorizing the nucleic acid by isolating nucleic acids wherein both termini of the double-stranded portion of said nucleic acid correctly hybridize to an oligonucleotide sequence by contacting a first set of oligonucleotide sequences with the nucleic acid population by:

(a) denaturing the nucleic acid population in the presence of the first set of oligonucleotide sequences covalently linked to a solid phase support to produce a single-stranded nucleic acid population and allowing the single-stranded nucleic acid to hybridise to the first set of oligonucleotide sequences, wherein each oligonucleotide sequence in said first set of oligonucleotide sequences has a pre-determined recognition sequence, the nucleic acid being categorized by its ability to correctly hybridize to oligonucleotide sequences having the recognition sequence, the recognition sequence being situated such that it recognizes a sequence in the portion of the nucleic acid which was double-stranded after digestion with the endonuclease;

(b) immobilizing those nucleic acids which correctly hybridise to the oligonucleotide sequence added to that well;

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(c) extending the correctly hybridised oligonucleotide sequences along the single-stranded portion of the immobilised nucleic acid to form double-stranded nucleic acid;

(d) denaturing the double-stranded nucleic acid and removing non-immobilised species to isolate the resulting immobilised single-stranded nucleic acid;

(e) contacting the immobilised single-stranded nucleic acid with a second set of oligonucleotide sequences, wherein each oligonucleotide sequence in said second set of oligonucleotide sequences has a pre-determined recognition sequence, the nucleic acid being categorized by its ability to correctly hybridize to oligonucleotide sequences having the recognition sequence, the recognition sequence being situated such that it recognizes a sequence in the portion of the nucleic acid which was double-stranded after digestion with the endonuclease;

(f) extending the correctly hybridised oligonucleotide sequences along the immobilised single-stranded nucleic acid to form double-stranded nucleic acid;

(g) denaturing the double-stranded nucleic acid; and

(h) isolating the resulting non-immobilised single-stranded nucleic acid.

REMARKS

Entry of the foregoing and further and favorable reconsideration of the subject application, in view of the following remarks and pursuant to 37 C.F.R. § 1.116, are respectfully requested. By the present amendment, claim 14 has been amended to indicate that the oligonucleotide sequences are covalently linked to a solid phase support. Support for this amendment may be found, at the very least, on page 9, lines 7-9, of the specification as filed. No new matter has been added by the foregoing amendment.

Entry of this Amendment is proper under 37 C.F.R. § 1.116 because the amendment places the application in condition for allowance for the reasons discussed herein; does not raise any new issue requiring further search and/or consideration because the amendments amplify issues previously discussed throughout prosecution; does not present any additional claims; and places the application in better form for an appeal, should an appeal be necessary. Entry of the Amendment is thus respectfully requested.

None of the prior art cited by the Examiner disclose or suggest the features of amended claim 14. Specifically, neither Rothberg et al, Dynal Catalog nor Hartley et al disclose or suggest covalently linking the primers (oligonucleotide sequences) to a solid phase support. Rothberg et al and the Dynal catalog disclose the use of a biotin/avidin system for the capture of nucleic acid fragments (Hartley et al does not disclose any system for the capture of nucleic acid fragments). The avidin component of the avidin/biotin system is prone to denaturation and decomposition, which adversely affects its performance. Covalently linking the primers (i.e. oligonucleotide sequences) to a solid phase support is advantageous over the prior art since the supports are more stable and

since the support provides a higher binding capacity than that of a biotin/avidin system. Greater stability allows for the use of more stringent washing conditions, improves the quality of the results and allows for longer term storage of the supports without loss of sample. In order to establish a *prima facie* case of obviousness, the prior art references, when taken together, much teach or suggest all of the claim limitations (MPEP Sec. 2142). In the present case, none of the cited references disclose or suggest the use of a solid phase support. Furthermore, it would not be obvious in view of the disclosures of Rothberg et al, Dynal Catalog and Hartley et al, and what was known in the art at the time the invention was made, to replace the biotin/avidin system of Rothberg et al and Dynal Catalog with the solid phase support used in the claimed invention. Therefore, the Examiner has not established a *prima facie* case of obviousness, and the claimed invention is not obvious in view of Rothberg et al, Dynal Catalog, or Hartley et al, either taken alone or together.

Applicants respectfully submit that all of claims 14-22 and 42-49 are now in condition for allowance. Reconsideration and withdrawal of the rejections of the claims under 35 U.S.C. § 103(a) are respectfully requested. Prompt reconsideration and allowance of the claims is believed to be next in order.

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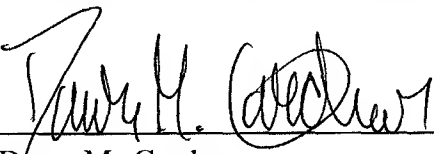
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Should the Examiner require anything further in order to place the application in better condition for allowance, he is invited to contact applicants representative at the telephone number below.

Respectfully submitted,

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